

# Comparison of Bayesian and Classical Analysis of Weibull Regression Model: A Simulation Study

## Bayesgil ve Klasik Weibull Regresyon Modelinin Karşılaştırılması: Bir Simülasyon Çalışması

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Geliş Tarihi/Received: 25.06.2010  
Kabul Tarihi/Accepted: 04.10.2010

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**ABSTRACT Objective:** The purpose of this study was to compare performances of classical Weibull Regression Model (WRM) and Bayesian-WRM under varying conditions using Monte Carlo simulations. **Material and Methods:** It was simulated the generated data by running for each of classical WRM and Bayesian-WRM under varying informative priors and sample sizes using our simulation algorithm. In simulation studies,  $n=50, 100$  and  $250$  were for sample sizes, and informative prior values using a normal prior distribution with  $\beta_p = 1, 1.5, 2$  and  $\sigma_p^2 = 0.1, 0.5$  was selected for  $\beta_1$ . For each situation, 1000 simulations were performed. **Results:** Bayesian-WRM with proper informative prior showed a good performance with too little bias. It was found out that bias of Bayesian-WRM increased while priors were becoming distant from reliability in all sample sizes. Furthermore, Bayesian-WRM obtained predictions with more little standard error than the classical WRM in both of small and big samples in the light of proper priors. **Conclusion:** In this simulation study, Bayesian-WRM showed better performance than classical method, when subjective data analysis performed by considering of expert opinions and historical knowledge about parameters. Consequently, Bayesian-WRM should be preferred in existence of reliable informative priors, in the contrast cases, classical WRM should be preferred.

**Key Words:** Bayes theorem; survival analysis; markov chains; computer simulation

**ÖZET Amaç:** Bu çalışmanın amacı, klasik Weibull regresyon modeli (WRM) ile Bayesgil-WRM yöntemlerini farklı koşullar altında Monte Carlo simülasyonlarıyla performanslarının karşılaştırılmasıdır. **Gereç ve Yöntemler:** Simülasyon algoritmamız kullanılarak, farklı açıklayıcı önsel bilgi ve örneklem hacimlerinde türetilen verilerle klasik WRM ile Bayesgil-WRM için simülasyonlar gerçekleştirildi. Simülasyon çalışmasında  $n = 50, 100, 250$  örneklem hacimleri ve  $\beta_1$  için  $\beta_p = 1, 1.5, 2$  ve  $\sigma_p^2 = 0.1, 0.5$  parametrelili normal önsel dağılımdan alınan açıklayıcı önsel bilgiler seçildi. Her bir durum için 1000 simülasyon gerçekleştirildi. **Bulgular:** Veriye uygun önsel bilgi kullanıldığında Bayesgil-WRM biraz daha iyi performans gösterdi. Tüm örnek hacimlerinde önsel bilgi güvenilirlikten uzaklaştıkça Bayesgil-WRM'nin yanlılığının arttığı belirlendi. Ayrıca küçük ve büyük örnek hacimlerinde ve veriye uygun önsel bilgilerle çalışıldığında Bayesgil-WRM'nin, klasik WRM'den daha küçük standart hatalı tahminler elde ettiği belirlendi. **Sonuç:** Bu simülasyon çalışmasında Bayesgil-WRM, parametreler hakkında uzman görüşleri ve daha önceki bilgiler ele alınarak subjektif veri analizi gerçekleştirildiğinde klasik yöntemden daha iyi performans gösterdi. Sonuç olarak Bayesgil-WRM'nin, güvenilir açıklayıcı önsel bilgi var olduğunda tercih edilmesi gerektiği aksi durumda klasik WRM'nin tercih edilebileceği önerilmektedir.

**Anahtar Kelimeler:** Bayes teoremi; sağkalım analizi; markov zincirleri; bilgisayar simülasyonu

Türkiye Klinikleri J Biostat 2011;3(1):8-13

The effect of covariates is proportional with respect to survival time in accelerated failure time (AFT) models. The Weibull regression model (WRM) is widely used as one of accelerated failure time models.

Because, it can take on different shapes and can be flexible to suit various applications.<sup>1</sup>

Bayesian analysis of survival data has received much recent attention due to advances in computational and modelling techniques.<sup>2</sup> Also, parametric survival models are applied using Bayesian approach. Bayesian approach provides inferences that are exact according to classical methods, and has the advantage in dealing with small sample over classical methods. In the present study, Bayesian-WRM was carried out using Bayesian approach based on varying conditions.

Bayesian methods consist of data and prior information. It generates conclusions based on the synthesis of new information from an observed data and historical knowledge or expert opinion. Therefore, Bayesian methods reflect subjective beliefs. Bayesian methods cannot be used for any modeling without using a prior distribution.<sup>2,3</sup>

Few works have been published on the Bayesian-WRM method. Calle et al.<sup>4</sup> analyzed data from sensory shelf-life studies. Wong et al.<sup>5</sup> used Bayesian-WRM to investigate the effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting active dentin caries in Chinese pre-school children. Sahu et al.<sup>6</sup> analyzed data from first and second recurrence of infection in kidney patients on dialysis using Bayesian-WRM with frailties. Abrams et al.<sup>7</sup> analyzed data from cancer clinical trial based on beliefs of clinicians and results available of published/unpublished trials and noninformative prior distributions using Bayesian-WRM.

In our study, we aimed to compare the performances of classical WRM and Bayesian-WRM by using Monte Carlo simulations under varying conditions.

## MATERIAL AND METHODS

### WEIBULL REGRESSION MODEL

Survival analysis investigates examines the relationship of the survival distribution to covariates.<sup>8</sup> Parametric survival models are known as the AFT model. These models can be linearized by taking logarithm:

$$\ln(t) = \beta_0 + \beta_1 x + \sigma \varepsilon$$

where  $t$  is a random variable denoting the survival time,  $x$  is a covariate,  $\beta_0$  and  $\beta_1$  are model parameters and  $\varepsilon$  is an error term. The baseline distribution of the error term can be specified as one of the exponential, log-normal, log-logistic, and Weibull distributions.<sup>1,9</sup>

The fundamental distributions that have been proposed for modeling survival are the exponential, Weibull and Gompertz distribution. The WRM based on Weibull distribution is the most widely used survival model for investigated the impact of other factors on survival. It is a parametric survival model and an AFT model that is one in which survival time is assumed to follow a known distribution.<sup>1</sup> The hazard function for the single covariate WRM is

$$h(t, x, \beta, \lambda) = \frac{\lambda t^{\lambda-1}}{(e^{\beta_0 + \beta_1 x})^\lambda}$$

where  $\lambda = 1/\sigma$ . The proportional hazards form of the function is

$$h(t, x, \beta, \lambda) = h_0(t) e^{\theta_1 x} \lambda \gamma t^{\lambda-1} e^{\beta_0 + \beta_1 x} \frac{\lambda t^{\lambda-1}}{(e^{\beta_0 + \beta_1 x})^\lambda}$$

where the baseline hazard function is  $h_0(t) = \lambda \gamma t^{\lambda-1}$ ,  $\gamma = e^{-\beta_0/\sigma} = e^{\theta_0}$  and  $\theta_1 = -\beta_1/\sigma$ . Although the parameter  $\sigma$  is a variance-like parameter on the log-time scale,  $\lambda = 1/\sigma$  is commonly called the shape parameter. Also  $\gamma$  is a scale parameter.<sup>1,9</sup>

The parameters of the Weibull probability distribution estimate by maximum likelihood. Maximum likelihood estimation consists of finding the values of the distribution parameters that maximize the log-likelihood of the data values. The log-likelihood function of the WRM is

$$L(\beta) = \sum_{i=1}^n c_i (-\ln(\sigma) + z_i) - e^{z_i}$$

where  $z_i = (\ln(t_i) - \mathbf{x}'_i \beta)/\sigma$ ,  $\mathbf{x}'_i = (x_{i0}, x_{i1}, \dots, x_{ip})$  and  $x_{i0} = 1$ . The likelihood equations are obtained by differentiating the log-likelihood function with respect to the unknown parameters and setting the expressions equal to zero.<sup>1,9</sup>

### BAYESIAN WEIBULL REGRESSION MODEL

Bayesian analysis generates based on the combining of new information from the observed data and previous knowledge or expert opinion.<sup>5</sup>

In classical approaches such as maximum likelihood for parameter estimation, inference is based on the likelihood of the data alone. In Bayesian models, the likelihood ( $L(\beta)$ ) of the observed data  $x$  given parameters  $\beta$  is used to recast the prior  $\pi(\beta_0)$ , with the updated knowledge summarized in a posterior density ( $\pi(\beta | x)$ ).<sup>8,10,11</sup> The relationship between these densities is

$$\pi(\beta|x) \propto L(\beta)p(\beta)$$

Thus, updated knowledge is a function of prior knowledge and the present data.<sup>2,3,8,10,11</sup>

The density function of Weibull distribution in terms of the parameterization  $\alpha=\log(\gamma)$  is  $f(t|\lambda, \alpha) = \lambda t^{\lambda-1} \exp(\alpha - \exp(\alpha) t^\lambda)$

The likelihood function of WRM for  $\lambda$  and  $\alpha$  parameters is specified by

$$L(\lambda, \alpha|t) = \prod_{i=1}^n f(t_i|\lambda, \alpha)^{v_i} S(t_i|\lambda, \alpha)^{1-v_i} = \lambda^{\sum_{i=1}^n v_i} \exp\{\alpha(\sum_{i=1}^n v_i) + \sum_{i=1}^n (v_i(\lambda - 1)\log(t_i) - t_i^\lambda \exp(\alpha))\}$$

where  $S(t|\lambda, \alpha) = \exp(-\exp(\alpha)t^\lambda)$  denoted Weibull survival function,  $t = (t_1, t_2, \dots, t_n)'$  is the independent identically distributed survival times, and  $v$  is the indicator variable.<sup>2</sup> If  $t_i > T_i$ , the  $i$ th data is censored and thus, indicator variable is

$$v_i = \begin{cases} 1, & t_i \leq T_i \\ 0, & t_i > T_i \end{cases}$$

When  $\lambda$  is assumed known, the conjugate prior for  $\exp(\alpha)$  the gamma prior. The joint conjugate prior is not available when  $(\lambda, \alpha)$  are both assumed unknown.<sup>2</sup> The joint posterior distribution of  $(\lambda, \alpha)$  is as follows:

$$\pi(\lambda, \alpha|n, t, v) \propto L(\lambda, \alpha|n, t, v)\pi(\lambda|\lambda_0, \kappa_0)\pi(\alpha|\mu_0, \sigma_0^2)$$

where  $N(\mu_0, \sigma_0^2)$  has the normal prior for  $\alpha$ , and  $\zeta(\lambda_0, \kappa_0)$  has a gamma prior for  $\lambda$ .

In the Bayesian-WRM, the joint posterior distribution for  $\lambda$  and  $\beta$  parameters is  $\pi(\beta, \lambda|n, t, x, v)$

$$\propto \lambda^{\lambda_0 + (\sum_{i=1}^n v_i) - 1} \exp\left\{ \sum_{i=1}^n (v_i x'_i \beta + v_i(\lambda - 1)\log(t_i) - t_i^\lambda \exp(x'_i \beta)) - \kappa_0 \lambda - \frac{1}{2}(\beta - \mu_0)' \Sigma_0^{-1} (\beta - \mu_0) \right\}$$

where  $N_p(\mu_0, \Sigma_0)$  is a prior for  $\beta$  and  $\alpha_i = x'_i \beta$ .<sup>2</sup>

In complex models, posterior densities can be difficult to work with directly. It is required that update of knowledge about the parameters. With Markov Chain Monte Carlo (MCMC) method, it is possible to generate samples from a posterior density and to use these samples to approximate expectations of quantities of interest. Gibbs sampler is a MCMC method, and a powerful simulation algorithm. Gibbs sampler can be efficient when the parameters are not highly dependent on each other and the full conditional distributions are easy to sample from.<sup>3,8,11,12</sup>

Gibbs sampler works as follows:<sup>2,3,12</sup>

- 1) Set  $m=0$  ( $m=1,2,\dots,M$ ), and choose an arbitrary initial value of  $\beta^{(0)} = \{\beta_1^{(0)}, \beta_2^{(0)}, \dots, \beta_p^{(0)}\}'$ .
- 2) Generate each component of  $\beta^{(m+1)} = \{\beta_1^{(m+1)}, \beta_2^{(m+1)}, \dots, \beta_p^{(m+1)}\}'$  as follows:
  - Draw  $\beta_1^{(m+1)}$  from  $\pi(\beta_1 | \beta_2^{(m)}, \dots, \beta_p^{(m)}, \mathbf{x})$
  - Draw  $\beta_2^{(m+1)}$  from  $\pi(\beta_2 | \beta_1^{(m+1)}, \beta_3^{(m)}, \dots, \beta_p^{(m)}, \mathbf{x})$
  - ... ..
  - Draw  $\beta_p^{(m+1)}$  from  $\pi(\beta_p | \beta_1^{(m+1)}, \beta_2^{(m+1)}, \dots, \beta_{p-1}^{(m+1)}, \mathbf{x})$

3) Set  $m=m+1$  and go to step 1.

In Bayesian analysis, elicitation of the prior plays also the most major role. Bayesian analysis cannot be used for any modeling without using a prior distribution. Bayesian analysis is used to noninformative or informative prior in inference. Informative prior obtains from previous studies. It is not dominated by the likelihood and is effective on the posterior distribution.<sup>3,13,14</sup>

### SIMULATION ALGORITHM

Our interest in this study was to compare the parameter estimates from WRM and Bayesian-WRM in different conditions. The models developed here have the same multiplicative structure. We used

a simulation algorithm for analyses. The probability models with one explanatory variable were used in simulations and the following step were applied to carry out the simulations.

We compared WRM and Bayesian-WRM with informative prior in this algorithm.

- 1) Set up a value of the model parameters ( $\beta_0$  and  $\beta_1$ )
- 2) Set up a value of the sample size.
- 3) The explanatory variable ( $x$ ) was generated from uniform distribution with (0,1) parameters.
- 4) Two variables ( $t_1$  and  $t_2$ ) were generated from exponential distribution with  $exp(x'_i\beta)$  and 1 parameters, respectively.
- 5) Survival time ( $t$ ) was denoted as  $\min(t_1, t_2)$ .
- 6) For uncensored data, if  $t_1 \leq t_2$ , uncensored was 1.
- 7) WRM and Bayesian-WRM were performed by using these steps.
- 8) The parameter estimates were recorded. 3th-7th steps were replicated 1000 times. Thus, 1000 different parameter estimates were obtained from the analyses.

In simulation studies,  $n=50, 100$  and  $250$  were for sample sizes.  $\beta_0=0.5$  and  $\beta_1=1$  were selected. In the algorithm, informative prior values using a normal prior distribution with  $\bar{\beta}_p = 1, 1.5, 2$  and  $\sigma_p^2 = 0.1, 0.5$  was selected for  $\beta_1$ , and informative prior values using a normal prior distribution with  $\bar{\beta}_{p_0} = 0.5$  and  $\sigma_{p_0}^2 = 0.5$  and  $= 0.1$  was selected for  $\beta_0$ .

Also, the gamma prior distribution parameters for  $\lambda$  were a  $\zeta(10^{-4}, 10^{-4})$ .

In this algorithm, the underlying assumption was that, after 2000 iterations, the chain would have reached its target distribution. Thus, we took a burn-in of 2000 samples and the posterior estimates were based on 10000 Markov chain samples.

Simulations and analyses were performed by using SAS macro programming language, and SAS LIFEREG and BLIFEREG procedures. For each situation, 1000 simulations were performed. After the analyses based on algorithm were performed, the mean of the 1000 different parameter estimates was calculated. It was evaluated that how the average of parameter estimates close to the value determined for  $\beta_1$  in step 1. Biases were calculated as  $\hat{\beta} - \beta$ .

## RESULTS

We simulated the generated data by running for each of WRM and Bayesian-WRM with informative prior using the simulation algorithm. The averaged values over the 1000 simulations were reported in Table 1 and Figure 1 for varying sample sizes. When sample size was increased, the parameter estimates obtained from WRM and Bayesian-WRM were small standard error. On condition that the best informative prior ( $\bar{\beta}_p = 1$  and  $\sigma_p^2 = 0.1, 0.5$ ), Bayesian-WRM had a better predictive performance than WRM for all of the sample sizes. Especially, for  $\bar{\beta}_p = 1$ , standard errors of parameter estimates obtained from Bayesian-WRM increased while variance of informative prior in-

**TABLE 1:** Posterior parameter estimate ( $\hat{\beta}_1$ ), bias and standard error obtained from 1000 Monte Carlo simulation for  $\beta_1=1$  and  $n=50, 100, 250$ ).

Method	Prior		n=50				n=100				n=250			
	$\bar{\beta}_p$	$\sigma_p^2$	$\hat{\beta}_1$	$\hat{\sigma}_{\hat{\beta}_1}$	Bias	p	$\hat{\beta}_1$	$\hat{\sigma}_{\hat{\beta}_1}$	Bias	p	$\hat{\beta}_1$	$\hat{\sigma}_{\hat{\beta}_1}$	Bias	p
WRM	-	-	1.1279	1.4838	0.1279	0.545	1.0344	0.9647	0.0344	0.722	1.0131	0.5812	0.0131	0.722
Bayesian-WRM	1	0.1	1.0028	0.3004	0.0028	0.948	1.0032	0.2898	0.0032	0.912	1.0150	0.2669	0.0150	0.375
	1	0.5	1.0464	0.5713	0.0464	0.568	1.0597	0.5099	0.0597	0.244	1.0506	0.4130	0.0516	0.054
	1.5	0.1	1.4609	0.3063	0.4609	<0.001	1.4409	0.2972	0.4409	<0.001	1.3823	0.2759	0.3823	<0.001
	1.5	0.5	1.3706	0.6000	0.3706	<0.001	1.3448	0.5371	0.3448	<0.001	1.2202	0.4301	0.2202	<0.001
	2	0.1	1.9372	0.3104	0.9372	<0.001	1.8906	0.3037	0.8906	<0.001	1.7718	0.2852	0.7718	<0.001
	2	0.5	1.7624	0.6279	0.7624	<0.001	1.6262	0.5643	0.6262	<0.001	1.4224	0.4460	0.4224	<0.001

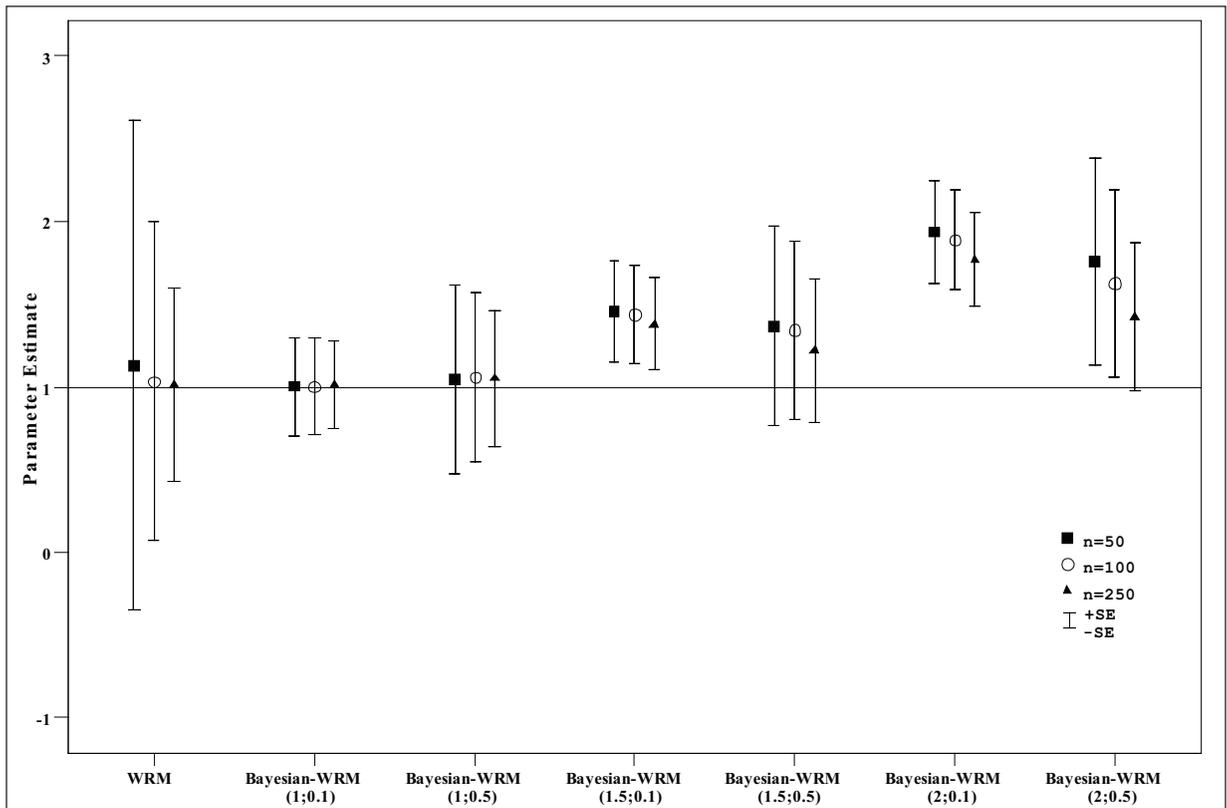


FIGURE 1:  $\hat{\beta}_1$  parameter estimates and standard errors (SE) obtained from 1000 Monte Carlo simulation for:  $\beta_1 = 1$  and  $n=50, 100, 250$  of WRM, and Bayesian-WRM.

creased. On condition that the improper informative prior ( $\bar{\beta}_p = 1.5, 2$ ), we found that bias of the parameter estimates increased in Bayesian-WRM according to simulation parameter. However, when sample size and/or variance of prior distribution increased, although prior information was improper, we found that the bias of the parameter estimates decreased.

While parameter estimates of WRM and Bayesian-WRM with  $\bar{\beta}_p = 1$  and  $\sigma_p^2 = 0.1, 0.5$  priors were convergence to simulation parameter according to two proportion t test ( $p > 0.05$ ), parameter estimates of Bayesian-WRM with  $\bar{\beta}_p = 1.5, 2$  and  $\sigma_p^2 = 0.1, 0.5$  priors were not convergence to simulation parameter ( $p < 0.001$ ).

In the Bayesian-WRM, Geweke diagnostic test and autocorrelations indicated a reasonably good mixing of the Markov chain ( $p > 0.05$ ).

## DISCUSSION

We compared across the WRM and Bayesian-WRM methods under varying sample sizes by

using Monte Carlo simulation method on the randomized censoring simulation data.

The Weibull distribution is a flexible right skewed distribution which is especially appropriate for modelling survival data.<sup>1,4,15</sup> The WRM is the most widely used for the analysis of survival data.

The Bayesian-WRM cannot be used for any modeling without using a prior distribution. Prior information plays the most crucial role in Bayesian-WRM. Calle et al.<sup>4</sup> and Ibrahim et al.<sup>2</sup> reported that Bayesian and classical approaches usually result in similar conclusions, when additional external information is not available. Abrams et al.<sup>7</sup> compared data from patients with tumours of the pelvic region using Bayesian-WRM based on clinical beliefs, the results of previous studies and reference prior distributions. They reported that Bayesian approach based on the results of previous studies extremely close to the results of the current study, but led to a reduction in the variance. Also they said that Bayesian approach yields a realistic assessment of the current evidence for a treatment.

Yin and Ibrahim<sup>16</sup> analyzed using Bayesian analysis with a simulation study for varying sample sizes, 1000 replications, 5000 Gibbs samples and 200 burn-in samples and a real data set from a melanoma clinical trial. They determined that the posterior standard deviation increases, as the censoring rate increases. Calle et al.<sup>4</sup> reported that the results obtained from the fat-free yogurt were used to construct a prior information in calculating the whole-fat yogurt posterior distributions, and they led to small improvements in the posterior distributions. Wong et al.<sup>5</sup> used Bayesian-WRM to investigate the effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting active dentin caries in Chinese pre-school children. They reported that there is a danger that the additional complexity of Bayesian methods could lead to improper data analysis if it is not used correctly. In our simulation study, we showed that prior information played the very crucial role in predicting simulation parameter. We showed that performance of Bayesian-WRM increased when proper prior information with small variance was used. In Bayesian-WRM, the bias of parameter estimate increased for using improper prior information and varying sample sizes. However, when improper prior information with small variance was used, the bias of parameter estimate increased. Gelman<sup>14</sup> said that prior distribution is a key part of Bayesian inference. They reported that with well-identified parameters and large sample sizes, reasonable cho-

ices of prior distributions will have minor effects on posterior inferences, and if the sample size is small or available data provide only indirect information about the parameters of interest, the prior distribution becomes more important. Gelfand and Mallick<sup>17</sup> said that Bayesian approach would be expected to provide more believable estimates of variability than under likelihood analysis for smaller data sets. Similarly, in our study, we found that the Bayesian approach had the best performance if proper informative prior was used for smaller data sets.

Although Bayesian-WRM is more advantage than WRM, in terms of flexibility of model-building for complex data, in our simulations, Bayesian-WRM used informative and proper prior information was more advantage than WRM. In every condition, informative and proper prior information should be used for analyzing data with Bayesian-WRM. In the situation that there was not available proper prior information, researchers should prefer a big sample size and prior distribution parameters with a big variance within prior distribution parameters from previous studies. As a result, Bayesian-WRM showed better performance than WRM, when subjective data analysis performed by considering of expert opinions and historical knowledge about parameters. Consequently, Bayesian-WRM should be preferred in existence of reliable or proper informative priors, in the contrast cases, WRM should be preferred.

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